In This Issue . . .

Gina Kolata

Altered Growth Requirements for Malignant Melanocytes

For several years, Barbara Gilchrest and her associates at the USDA Human Nutrition Research Center of Aging at Tufts University have been working on a system for the growth of human melanocytes. They decided, says Gilchrest, to use their system to compare the relative responsiveness of normal human melanocytes and melanoma cells to substances that promote cell growth. Gilchrest and her colleagues Philip Gordon, Valori Treloar, and Michael Vrabel report in this issue that melanoma cells seem to be unresponsive to two substances that promote growth of normal melanocytes in culture.

Gilchrest explains that the particular advantage of their system for growing melanocytes is that, unlike many other culture systems, it does not require phorbol esters, which promote the malignant conversion of cultured cells. Using their cell culture system, Gilchrest and her associates sought to determine whether melanocyte growth factor, a substance produced by the hypothalamus that is a potent growth stimulator of normal human melanocytes, affects the growth of melanoma cells. They find that it does not.

This observation is important because one hypothesis to explain malignant transformation is that malignant cells become independent of normal growth controls when they begin manufacturing for themselves growth factors that normally are supplied to them. If this were so for melanoma cells, they might be producing (endogenous) melanocyte growth factor and might not respond when the factor is supplied to them because all of their receptors are saturated. Gilchrest suggests, then, that "either the cells are making it themselves or they are making a very similar factor."

Another finding is that agents that stimulate cyclic AMP, which are a mainstay of in vitro cell growth systems and which cause normal melanoma cells to proliferate, have little or no effect on melanoma cells. "Cyclic AMP regulation may be important in the pathway converting a melanocyte to melanoma cells," Gilchrest suggests.

Both of these findings could "open the door to therapeutic approaches," Gilchrest says. It might eventually be possible, for example, to block melanoma cells' production of growth-stimulating factors or to intervene in the cyclic AMP pathways of malignant cells. Gilchrest and many others are now actively pursuing these lines of research.

Spores—Not Mycelia—Produce Pustules

Alfred Hernandez, now in private practice in Saratoga, Florida, Ronald Reece, now in private practice in Redding, California, and Albert Zucker, now in New York, noticed that dermatophyte infections of the scalp are associated with pustules and that dermatophyte infections elsewhere are associated with scales. According to Reece, "We asked ourselves, what could possibly be the reason?" In this issue, the investigators propose an answer.

In fungal infections of the scalp, there is a predominance of spores, and in fungal infections of the skin, mycelia predominate, Reece notes. So, he and his colleagues proposed, there may be a relationship between spores and pustules. When the researchers put spores of the fungus *Trichophyton mentagrophytes* on guinea pig skin, pustules formed. Mycelia, on the other hand, induced a mild lymphocytic infiltrate when applied to guinea pig skin.

The investigators then measured complement activation by spores and mycelia in vitro because complement is a chemoattractant for polymorphonuclear leukocytes. Spores, the investigators report, generate twice as much complement as mycelia at concentrations of fungus thought to be biologically relevant.

Because the cellular constituents of spores are largely similar to those of mycelia, the difference between the immune reaction to spores and mycelia may be that spores have a greater surface area, Reece and his colleagues suggest.

Relating Essential Fatty Acids and Acne

Recently, a group of researchers from the University of Iowa College of Medicine proposed a hypothesis relating essential fatty acids and acne. In this issue, the investigators, Mary Ellen Stewart, Marcia Owen Grahek, Linda Cambier, Philip Wertz, and Donald Downing report experimental evidence that is consistent with their hypothesis.

"When we started, we knew that individuals with acne tend to have higher rates of sebum production than individuals without acne," says Stewart. "We also knew that individuals with acne have less linoleate in their sebum than individuals without acne. We speculated that these facts may be related. Our hypothesis was that the linoleate concentration in human sebum depends on 1) the quantity of linoleic acid present in each sebaceous cell at the commencement of its differentiation and 2) on the extent to which this initial endowment is diluted by the subsequent endogenous synthesis of lipid in *each* sebaceous cell."

Stewart emphasizes that she and her colleagues are considering sebum synthesis per cell rather than the rate of sebum production per unit of skin.

"Dividing cells are on the periphery of the sebaceous gland and

0022-202X/86/$03.50

the cells move into the center as they mature," says Stewart. "Our idea is that the cells that are dividing on the periphery can pick up essential fatty acids such as linoleic acid and incorporate them into their membranes. At the end of their lifetime, when the cells break down, the linoleic acid becomes part of the sebaceous lipids. The more sebum there is, the more the linoleic acid is diluted." Thus the amount of linoleic acid in sebum is an indicator of the relative amount of sebum being produced.

In the *JID* paper, the researchers present data from their studies of prepubertal children and young adults indicating that sebum fatty acid composition may change as sebaceous gland activity changes and that sebum fatty acids can be incorporated into epidermal lipids. In particular, they found that the production of linoleate in sebaceous wax esters was inversely proportional to wax ester secretion rates.

They are still left with the question of how linoleate-deficient sebum might be related to the pathogenesis of acne. The group suggests that when the sebum in a follicle is deficient in linoleic acid, sebaceous fatty acids may replace linoleic acid. The skin in areas where sebaceous glands produce large amounts of sebum may suffer from a localized essential fatty acid deficiency. This deficiency might make it more likely that an acne lesion will form.

Stewart and her colleagues hope that a better understanding of how sebum is related to acne might lead to some form of prevention.

Possible Animal Model for Anhidrotic Ectodermal Dysplasia

A sex-linked mutation in the mouse shares clinical features with the human sex-linked genetic disorder, anhidrotic ectodermal dysplasia. In this issue, Stan Blecher of the University of Guelph presents evidence that, he says, "is one brick in building up the viewpoint that the mouse condition and the human condition are homologous—have the same evolutionary genetic origin."

Blecher holds to a viewpoint attributed to Susumu Ohno of City of Hope Medical Center in Duarte, California that the X-chromosome in humans is very similar to the X-chromosome in other mammals. Thus, Blecher concludes, "any gene on the human X-chromosome might be on the X-chromosome in other mammals." In particular, there might be an X-linked condition of mice that resembles anhidrotic ectodermal dysplasia.

The X-linked mouse mutation known as Tabby seemed to be a good candidate. Blecher reports in this issue that mice with the Tabby mutation lack sweat glands. If the Tabby mutation is indeed like the human genetic disease, then study of these mice could lead to an understanding of biochemical abnormalities in the human condition and also possibly to establishment of a possible prenatal diagnosis and, perhaps, to managing the care of affected patients.